Amended claims 36, 41, 44, 45, and 46 are fully supported by the specification of the present application, see, *e.g.*, page 70, line 10 to page 78, line 23 of the specification, and do not represent new subject matter. Claims 26-29, 33-41, 44-47, 53, 54, 65-79, and 87-90 will therefore be pending upon entry of this Amendment. The amendments and remarks made herein narrow the issues on appeal and are designed to place the case in condition for allowance. As such, Applicants respectfully request that the amendments and remarks made herein be entered and fully considered.

I. Rejection of Claims 37-39, 55-64, and 80-82 Under 35 U.S.C. § 112, ¶1-Enablement

Claims 37-39, 55-64 and 80-82 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Examiner contends that the specification fails to provide enablement for *any* substantially purified antibody that specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein the extracellular domain *comprises*: (1) amino acid residues 21 to 269 of SEQ ID NO:3; (2) an immunoglobulin-like domain; and (3) an immunoglobulin-like domain comprising amino acid residues 48 to 88 or 134 to 180 of SEQ ID NO:3 (*emphasis is the Examiner's*). Likewise, the Examiner contends that the specification fails to provide enablement for (4) *any pharmaceutical composition* comprising the composition comprising *any* substantially purified antibody... (*emphasis is the Examiner's*).

In particular, the Examiner contends that the term "comprises" expands the extracellular domain or the immunoglobulin-like domain of the amino acid sequence of SEQ ID NO:3 in addition to the amino acid residues already recited in SEQ ID NO:3. Moreover, the Examiner contends that there is insufficient guidance as to the binding specificity and the epitope to which the antibody recited in claims 37-39 binds. For the reasons detailed below, Applicants respectfully assert that the rejection 35 U.S.C. § 112, first paragraph, for lack of enablement cannot stand and should be withdrawn.

Applicants have cancelled claims 55-64 and 80-82, which describe pharmaceutical compositions. While in no way acceding to the Examiner's contention, the cancellation of claims 55-64 and 80-82 obviates this rejection with respect to those claims.

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics, Inc.* 857 F. 2d 778, 8 U.S.P.Q. 2d 1217 (Fed. Cir. 1988). Enablement is not precluded even if some experimentation is necessary. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F. 2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). The Court of Appeals for the Federal Circuit has determined that experimentation, though laborious, is not undue experimentation where the specification provides a reasonable amount of guidance. *In re Wands*, 858 F. 2d 731 (Fed. Cir. 1988). In the present instance, the specification provides one of ordinary skill in the art with sufficient guidance to meet the enablement requirements of 35 U.S.C. §112, ¶1, with respect to rejected claims 37-39. Therefore, as explained below, the claimed invention is enabled within the meaning of 35 U.S.C. §112, ¶1 (enablement).

Applicants respectfully assert that the specification of the present application coupled with information known as of the effective filing date of the present application provides sufficient guidance to enable one of skill in the art to make and use the antibodies or fragments recited in claims 37-39 without undue experimentation. First, the specification of the present application explicitly teaches methods of making, isolating and identifying antibodies or fragments thereof that specifically bind to SEQ ID NO:3, including the extracellular domain of SEQ ID NO:3, wherein the extracellular domain comprises specific amino acid residues or an immunoglobulin-like domain. See, *e.g.*, page 69, line 23 to page 73, line 19, page 94, lines 3-14, and page 94, line 27 to page 96, line 8 of the specification of the present application. Moreover, techniques for making, isolating and identifying antibodies or fragments thereof that specifically bind to SEQ ID NO:3, including the extracellular domain of SEQ ID NO:3, wherein the extracellular domain comprises specific amino acid residues or an immunoglobulin-like domain, were well-known in the art at the time the present application was filed.

The specification of the present application fully enables one of skill in the art to make and use an antibody that specifically binds to an extracellular domain of SEQ ID NO:3 "comprising" specific amino acid residues of SEQ ID NO:3 or an immunoglobulin-like domain present within SEQ ID NO:3. Although use of the open ended term "comprising" in claims 37-39 expands the extracellular domain or the immunoglobulin-like domain of the amino acid sequence of SEQ ID NO:3 to include additional amino acids, Applicants have enabled manufacture and use of antibodies which are capable of binding to said additional amino acids.

As defined in the present specification (e.g., at page 71), epitopes encompassed by the antigenic peptide (e.g., SEQ ID NO:3) are regions that are located on the surface of the protein, *e.g.*, hydrophilic regions. The antibodies of the present invention are capable of binding to the epitopic regions of SEQ ID NO:3. While the language of the present claims ("comprises") may encompass regions outside of specifically described domains (such as residues 21 to 269 and :an immunoglobulin-like domain"), the skilled artisan, using the teachings of the present specification and known in the field at the time of filing, can easily recognize that antibodies possess no utility useless if they are unable to bind to their corresponding antigen (e.g., at an epitopic region). Therefore, the skilled artisan can easily determine, without undue experimentation, which regions of SEQ ID NO:3, *including those outside the specifically defined domains* would be capable of being bound by the antibodies of the present invention. For instance, an intracellular domain of SEQ ID NO:3, as determined by the present specification (e.g., by the hydropathy plots of the figures) would not be bound by an antibody of the present invention, and is quickly recognized by the ordinarily skilled artisan as, practically speaking, outside the scope of such claims as 36.

Moreover, contrary to the Examiner's contention, Applicants respectfully submit that the specification of the present application provides sufficient guidance regarding the binding specificity of an antibody or fragment thereof that specifically binds to an extracellular domain of SEQ ID NO:3, wherein the extracellular domain comprises specific amino acid residues or an immunoglobulin-like domain, and sufficient guidance regarding the epitope to which such an antibody or antibody fragment binds, to enable one of skill in the art to make and use such an antibody or antibody fragment without undue experimentation. The specification of the present application teaches that hydrophilic regions of glycoprotein VI (SEQ ID NO:3) such as, *e.g.*, the extracellular domain of glycoprotein VI, can be used as epitopes and that such epitopes may be denatured or partially denatured. See, *e.g.*, page 69, lines 31-35 of the specification of the present application. The specification also teaches methods of producing and identifying antibodies or fragments thereof that specifically bind to said epitopes. See, *e.g.*, page 69, line 23 to page 73, line 19, 77, lines 4-23, page 94, lines 3-14, and page 94, line 27 to page 96, line 8 of the specification of the present application.

Moreover, Applicants respectfully assert that given the fact that the knowledge in the field of antibodies is well-characterized, the specification of the present application provides sufficient guidance regarding the binding specificity of an antibody or fragment thereof recited in claims 37-39 and the epitope to which such antibody or fragment binds. Accordingly,

Applicants submit that the specification coupled with information well-known in the art as of the effective filing date of the present application regarding antibodies and epitopes fully enables one of skill in the art to make and use the antibodies and fragments thereof recited in claims 37-39 without undue experimentation.

In view of the foregoing, Applicants respectfully assert that the rejection under 35 U.S.C. § 112, first paragraph, for lack of enablement support cannot stand and should be withdrawn.

II. Rejection of Claims 37-39, 55-64, and 80-82 Under 35 U.S.C. § 112, ¶1- Written Description

Claims 37-39, 55-64 and 80-82 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner contends that the specification fails to provide written description support for *any* substantially purified antibody that specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein the extracellular domain *comprises*: (1) amino acid residues 21 to 269 of SEQ ID NO:3; (2) an immunoglobulin-like domain; and (3) an immunoglobulin-like domain comprising amino acid residues 48 to 88 or 134 to 180 of SEQ ID NO:3 (*emphasis is the Examiner's*). Likewise, the Examiner contends that the specification fails to provide written description support for (4) *any pharmaceutical composition* comprising the composition comprising *any* substantially purified antibody... (*emphasis is the Examiner's*).

In particular, the Examiner contends that the term "comprises" expands the extracellular domain or the immunoglobulin-like domain of the amino acid sequence of SEQ ID NO:3 in addition to the amino acid residues already recited in SEQ ID NO:3. Moreover, the Examiner contends that there is insufficient guidance as to the binding specificity and the epitope to which the antibody recited in claims 37-39 binds. For the reasons detailed below, Applicants respectfully assert that the rejection 35 U.S.C. § 112, first paragraph, for lack of written description support cannot stand and should be withdrawn.

Applicants have cancelled claims 55-64 and 80-82, which describe pharmaceutical compositions. While in no way acceding to the Examiner's contention, the cancellation of claims 55-64 and 80-82 obviates this rejection with respect to those claims.

"If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly

described in the specification, then the adequate description requirement is met." Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, P1, "Written Description" Requirement, Federal Register, Vol. 66, No. 4, page 1106, Friday, January 5, 2001.

Applicants respectfully assert that the specification coupled with information well-known in the art as of the effective date of the present application would reasonably convey to one of skill in the art that Applicants were in possession of the antibodies recited in claims 37-39. First, Applicants respectfully assert that there is, indeed, written description support in the specification of the present application for a substantially purified antibody or fragment thereof that specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein the extracellular domain comprises specific amino acid residues of SEQ ID NO:3 or an immunoglobulin-like domain present in SEQ ID NO:3. Applicants direct the Examiner's attention to page 11, line 35 to page 12, line 8, page 19, line 28 to page 20, line 2, and page 76, lines 18-27 of the specification of the present application for support of claims 37-39.

The structure of the antigen-binding sites of the antibodies recited in claims 37-39 are conventional to one of skill in the art. The antibodies recited in claims 37-39 have the structural characteristics of the various types of antibodies well-known to one of skill in the art including those disclosed in the specification of the present application on page 70, lines 11-20. According to the Synopsis of Application of Written Description Guidelines, at page 59, available at http://www.uspto.gov/web/patents/guides.htm ("Application Guidelines"), "[t]he general knowledge in the art is such that antibodies are structurally well characterized." Moreover, as previously stated in the Amendment Under 37 C.F.R. § 1.111, filed September 26, 2002, methods for making and identifying antibodies that specifically bind to human glycoprotein VI or an extracellular domain thereof are described in the specification of the present application and were well-known as of the effective filing date of the present application. See, *e.g.*, page 69, line 23 to page 73, line 19, page 94, lines 3-14, and page 94, line 27 to page 96, line 8 of the specification of the present application, and Chapter 14 of Harlow et al., eds, 1988, Antibodies A Laboratory Manual, Cold Spring Harbor, New York. Thus, Applicants respectfully assert that, given the state of the art of antibody production and the information in the specification, the structures of the antibodies recited in claims 37-39 are sufficiently described to meet the written description requirements.

Regarding the Examiner's concern about the "comprising" language of claims 37-39, as discussed above, the ordinarily skilled artisan can easily recognize from the present specification which portions of SEQ ID NO:3 are capable of being bound by the antibodies of the invention.

Therefore, the ordinarily skilled artisan can easily arrive at the full range of species members that populate the scope of claims 37-39 by using the guidance of the present invention, and ruling out regions of SEQ ID NO:3 that are incapable of being bound by antibodies (e.g., intracellular regions of the protein, or regions of the protein that are outside or on the surface of the cell, yet sterically are incapable of being bound).

In view of the foregoing, Applicants respectfully assert that the rejection under 35 U.S.C. § 112, first paragraph, for lack of written description support cannot stand and should be withdrawn.

III. Rejection of Claims 36, 45, 46, and 71-73 Under 35 U.S.C. § 112, ¶2

Claims 36, 45, 46 and 71-73 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards the invention. The Examiner contends that the recitation of the term "which is conjugated to a therapeutic moiety" in claims 45 and 72 is improper because a dependent claim should be narrower in scope than the claim from which it depends. The Examiner also contends that the recitation of the term "which is linked to a detectable substance" in claims 46 and 73 is improper because a dependent claim should be narrower in scope than the claim from which it depends. For the reasons detailed below, the rejection under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn.

Applicants respectfully assert that dependent claims 45, 46, 72 and 73 are proper. The recitation of the term "which is conjugated to a therapeutic moiety" in dependent claims 45 and 72, and the recitation of the term "which is linked to a detectable substance" in dependent claims 46 and 73, amount to additional elements which narrow the scope of independent claims 36 and 71. In other words, independent claims 36 and 71 are broader *without* the addition of the elements "which is conjugated to a therapeutic moiety" and "which is linked to a detectable substance," than they are *with* the elements (as in dependent claims 45, 46, 72, and 73).

The antibody of claim 36, for instance, does not need to be conjugated to a therapeutic moiety in order to be within the scope of that claim. Likewise, the antibody of claim 71, need not be coupled to a detectable substance (such as those given as examples on page 76, line 4 of the present specification (various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials)) in order to be within the scope of that claim.

With respect to independent claims 36 and 71, the Examiner has not provided any reasoning for rejecting these claims. Therefore, Applicants respectfully assert that the rejection under 35 U.S.C. § 112, second paragraph, cannot stand and should be withdrawn.

IV. Rejection of Claims 24-25, 36-38, 40, 44, 55, 61, and 62 Under 35 U.S.C. § 102(b)

Claims 24-25, 36-38, 40, 44, 55, 61 and 62 are rejected under 35 U.S.C. § 102(b) as being anticipated by Sugiyama *et al.*, 1987, Blood 69(6):1712-1720 (hereinafter "Sugiyama"). Claims 24-25, 36-38, 40, 44, 55, 61 and 62 are also rejected under 35 U.S.C. § 102(b) as being anticipated by Gibbins *et al.*, 1997, FEBS Letters 413:225-259 (hereinafter "Gibbins").

The Examiner contends that Sugiyama teaches: (1) a composition of a substantially purified antibody, namely a human auto-antibody, and a $F(ab')_2$ fragment thereof that specifically binds to a collagen receptor with an apparent molecular weight of 62 KDa which is expressed by platelets, wherein the antibody and $F(ab')_2$ fragment are in phosphate buffered saline ("PBS"), a pharmaceutically acceptable carrier; and (2) methods of purifying an antibody such as IgG and a $F(ab')_2$ fragment thereof. The Examiner contends that Gibbins teaches a composition of a substantially purified antibody, namely a human auto-antibody from a patient with autoimmune thrombocytopenia, and a $F(ab')_2$ fragment thereof that specifically binds to glycoprotein VI, a protein of approximately 60 KDa which is expressed by platelets, wherein the antibody and $F(ab')_2$ fragment are in a Tris-HCl buffered solution, a pharmaceutically acceptable carrier. The Examiner contends that the collagen receptor to which the antibodies described in Sugiyama and Gibbins bind appears to be the same as the amino acid sequence of SEQ ID NO:3 which is predicted to be approximately 62 KDa. The Examiner also contends that the antibodies described by Sugiyama and Gibbins inherently bind to amino acid residues 21 to 269 of SEQ ID NO:3.

As discussed herein, Applicants have cancelled claims 24, 25, 55, 61, and 62, thereby obviating the present rejection with respect to those claims. For the reasons detailed below, Applicants respectfully assert that the rejections of remaining claims 36-38, 40, and 44 under 35 U.S.C. § 102(b) cannot stand and should be withdrawn.

It is axiomatic that for a prior art reference to anticipate a claimed invention under 35 U.S.C. § 102(b), it has to meet every element of the claimed invention. *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 231 U.S.P.Q. 81, 91 (Fed. Cir. 1986), cert. denied, 480 U.S. 947 (1987).

Applicants respectfully assert that the recitation of term "substantially purified" in independent claim 36 is sufficient in view of the definition provided in the specification of the present application for the term to convey the purity of the antibody. The specification of the present application defines the term "substantially purified" as an antibody composition contains no more than 30% (by dry weight) of contaminating antibodies. See, *e.g.*, page 71, lines 13-18 of the specification for this definition. In other words, the antibody recited in claim 36 represents at least 70% of the total antibodies of the composition. However, in order to expedite the prosecution of the present application and without conceding to the validity of the Examiner's rejection, Applicants have amended independent claim 36 to specifically recite that the antibody represents at least 70% of the composition.

Neither Sugiyama nor Gibbins teach an antibody or a composition comprising antibody or fragment thereof that specifically binds to SEQ ID NO:3 or an extracellular domain thereof, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC as Accession Number 207180, wherein the antibody purified and represents at least 70% of the total antibodies as recited in claim 36.

As previously discussed in the Amendment Under 37 C.F.R. § 1.111 filed on September 26, 2002, Sugiyama describes the immunoprecipitation of a group of polypeptides, including a predominant 62 KDa (using reducing conditions) polypeptide and at least four other platelet polypeptides using bulk IgG obtained from a human patient with idiopathic thrombocytopenic purpura. Sugiyama points out that the relationship, if any, between this group of polypeptides is unknown. Sugiyama also describes the ability of $F(ab')_2$ fragments produced from the human patient's bulk IgG to induce platelet aggregation and to inhibit platelet aggregation induced either by collagen or the patient's IgG. Sugiyama points out that it is unclear whether a single antibody or multiple antibodies with the patient's IgG mixture is/are responsible for the observed platelet aggregation activity. Gibbins uses the bulk human IgG mixture of Sugiyama and Fc receptor γ- chain ("FcR γ- chain") to demonstrate the constitutive association of GPVI with the FcR γ- chain. Gibbins also describes the tyrosine phosphorylation of the GPVI-associated FcR γ- chain and Syk in response to GPVI cross-linking mediated by $F(ab')_2$ fragments of the human bulk IgG preparation of Sugiyama.

Contrary to the Examiner's contentions, neither Sugiyama nor Gibbins teach how to purify the antibody that specifically binds to glycoprotein VI. Rather, Sugiyama and Gibbins merely provide methods for isolating total, bulk IgG from human patient with idiopathic thrombocytopenic purpura. The total IgG isolated from such a patient will contain multiple

IgGs, *i.e.*, contaminating antibodies. Thus, neither does Sugiyama or Gibbins teach a substantially purified antibody or a composition comprising a substantially purified antibody or a fragment thereof which specifically binds to GPVI or an extracellular domain thereof, wherein the antibody represents at least 70% of the total antibodies. Accordingly, neither Sugiyama nor Gibbins meet every element of the presently claimed invention, and therefore, do not anticipate claims 36-38, 40, and 44.

In view of the foregoing, Applicants respectfully assert that the rejection under 35 U.S.C. § 102(b) cannot stand and should be withdrawn.

V. Rejection of Claims 24, 36, 45-47, 54, 56, 63, 64, and 83-86 Under 35 U.S.C. § 103(a)

Claims 24, 36, 45-47, 54, 56, 63 and 64 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sugiyama or Gibbins each in view of Harlow et al., In: Antibodies a Laboratory Manual, 1988, Cold Spring Harbor Laboratory Publication, Cold Spring Harbor, NY, pages 321-358 (hereinafter "Harlow") or U.S. Patent No. 5,877,289 to Thorpe et al. ("Thorpe"). The Examiner contends that: (1) Sugiyama teaches a composition comprising a substantially purified antibody, namely a human auto-antibody, and a $F(ab')_2$ fragment thereof that specifically binds to a collagen receptor with apparent molecular weight of 62 KDa which is expressed by platelets; (2) Gibbins teaches a composition comprising a substantially purified antibody, namely a human auto-antibody from a patient with autoimmune thrombocytopenia, and a $F(ab')_2$ fragment thereof that specifically binds to a glycoprotein VI, a protein of approximately 60 KDa which is expressed by platelets; (3) Harlow teaches methods of labeling any antibody with a detectable substance; and (4) Thorpe teaches antibodies conjugated to a diagnostic agent or therapeutic agent and kits comprising antibodies conjugated to such agents.

The Examiner concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to link or conjugate the antibody taught by Sugiyama or Gibbins to a detectable substance or a therapeutic agent. The Examiner also concludes that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce kits comprising the antibody taught by Sugiyama or Gibbins conjugated to a detectable substance or a therapeutic agent.

As discussed herein, Applicants have cancelled claims 24, 54, 56, 63, 64, and 83-86, thereby obviating the present rejection with respect to those claims. For the reasons detailed

below, Applicants respectfully assert that the rejections of remaining claims 36 and 45-47 under 35 U.S.C. § 103(a) cannot stand and should be withdrawn.

A finding of obviousness requires a determination of the scope and content of the prior art, the level of ordinary skill in the art, the differences between the claimed subject matter and the prior art, and whether the differences are such that the subject matter as a whole would have been obvious to one of ordinary skill in the art at the time the invention was made. *Graham v. Deere* 383 U.S. 1 (1996). The proper inquiry is whether the art suggests the invention, and whether the art provides one of ordinary skill in the art with a reasonable expectation of success. *In re O'Farrell* 853 F.2d 894, 7 U.S.P.Q. 2d 1673 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art and not in the Appellants' disclosure. *In re Vaeck* 947 F.2d 488, 20 U.S.P.Q. 2d 1438 (Fed. Cir. 1991).

Obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination", and "teachings of references can be combined only if there is some suggestion or incentive to do so." *In re Fine* 837 F.2d 1071, 1075 (Fed. Cir. 1988).

As discussed above, neither Sugiyama nor Gibbins teach an antibody or a composition comprising an antibody or a fragment thereof which specifically binds to a polypeptide comprising an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein the antibody is substantially purified and the antibody represents at least 70% of the total antibodies. Further, neither Sugiyama nor Gibbins suggests or provides any motivation, let alone a reasonable expectation of success, that such an antibody can be made. Accordingly, neither Sugiyama nor Gibbins, alone or in combination, renders obvious the claimed invention.

The deficiencies in Sugiyama and Gibbins are not cured by Harlow nor Thorpe, alone or in combination. Harlow teaches methods of detectably labeling an antibody, and Thorpe teaches methods of the conjugation of antibodies to a diagnostic or therapeutic agent. Neither Harlow nor Thorpe teaches, suggests or provides any motivation for the production of an antibody or a composition comprising an antibody or a fragment thereof which specifically binds to a polypeptide comprising an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein the antibody is substantially purified and the antibody represents at least 70% of the total antibodies. Accordingly, the combination of Sugiyama, Gibbins, Harlow and Thorpe does not rise to the level of suggesting or providing motivation the claimed invention. Thus, the threshold inquiry of the test for determining whether a claimed invention is obvious is not met.

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Claims 24 and 83-86 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sugiyama or Gibbins. The Examiner contends that: (1) Sugiyama teaches a method of purifying an antibody for use in a composition comprising various platelet inhibitors such as the ones shown in Table 2 of Sugiyama; and (2) Gibbins teaches a method of purifying an antibody for use in a composition comprising the reference anti-glycoprotein VI antibody and platelet lysate. As discussed above, Applicants have cancelled claims 24 and 83-86, thereby obviating the present rejection with respect to those claims.

In view of the foregoing, Applicants respectfully assert that the rejections under 35 U.S.C. § 103(a) cannot stand and should be withdrawn.

CONCLUSION

Applicants respectfully request entry and consideration of the foregoing remarks. Applicants believe that all of the present claims meet all of the requirements for patentability. Withdrawal of all rejections is requested.

If any issues remain, the Examiner is requested to telephone the undersigned at (617) 761-6865.

April 17, 2003	MILLENNIUM PHARMACEUTICALS, INC. By _____ Paul J. Pagliarani Registration No. 52,488 75 Sidney Street Cambridge, MA 02139 Telephone - 617-761-6865 Facsimile - 617-551-8820

EXHIBIT A
A MARKED UP VERSION OF THE CLAIMS
IN U.S. APPLICATION SERIAL NO.: 09/503,387
ATTORNEY DOCKET NO.: MBIO99-057CP2M

36. (Amended) A substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein said antibody represents at least 70% of total antibodies in the antibody composition.

41. (Amended) [The antibody of claim 36 which is] A substantially purified antibody which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

44. (Amended) The antibody of claim 36 or 41 which is a human antibody.

45. (Amended) The antibody of claim 36 or 41 which is conjugated to a therapeutic moiety.

46. (Amended) The antibody of claim 36 or 41 which is linked to a detectable substance.

EXHIBIT B
PENDING CLAIMS UPON ENTRY OF
THE AMENDMENT FILED APRIL 17, 2003
IN U.S. APPLICATION SERIAL NO. 09/503,387
ATTORNEY DOCKET NO.: MBIO99-057CP2M

26. A substantially purified non-human antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180.

27. A substantially purified non-human monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180.

28. The antibody of claim 27 which is a humanized antibody.

29. A monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180.

33. A monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180, which antibody is conjugated to a therapeutic moiety.

34. A monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180, which antibody is linked to a detectable substance.

35. The antibody of claim 34, wherein the detectable substance is selected from the group consisting of an enzyme, a prosthetic group, a fluorescent material, a luminescent material, a bioluminescent material, and a radioactive material.

36. A substantially purified antibody or a fragment thereof which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein said antibody represents at least 70% of total antibodies in the antibody composition.

37. The antibody of claim 36, wherein the extracellular domain comprises amino acid residues 21 to 269 of SEQ ID NO:3.

38. The antibody of claim 36, wherein the extracellular domain comprises an immunoglobulin-like domain.

39. The antibody of claim 38, wherein the immunoglobulin-like domain comprises amino acid residues 48 to 88 or 134 to 180 of SEQ ID NO:3.

40. The antibody of claim 36 which is a polyclonal antibody.

41. A substantially purified antibody which specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3, wherein the antibody is a monoclonal antibody, a chimeric antibody or a humanized antibody.

44. The antibody of claim 36 or 41 which is a human antibody.

45. The antibody of claim 36 or 41 which is conjugated to a therapeutic moiety.

46. The antibody of claim 36 or 41 which is linked to a detectable substance.

47. The antibody of claim 46, wherein the detectable substance is selected from the group consisting of an enzyme, a prosthetic group, a fluorescent material, a luminescent material, a bioluminescent material, and a radioactive material.

53. A kit comprising an antibody or fragment thereof as in claim 34, and instructions for use.

54. A kit comprising an antibody or fragment thereof as in claim 46, and instructions for use.

65. A method of making an antibody that specifically recognizes GPVI, the method comprising:

a) immunizing a mammal with a polypeptide comprising the amino acid sequence of SEQ ID NO:3, the amino acid sequence encoded by the cDNA insert of the plasmid deposited with ATCC as Accession Number 207180; and

b) collecting a sample from the mammal that contains an antibody that specifically recognizes GPVI.

66. The method of claim 65 wherein the polypeptide is recombinantly produced.

67. The method of claim 65 which further comprises purifying antibodies from the sample.

68. The method of claim 65 which further comprises isolating a monoclonal antibody-producing cell from the mammal.

69. The method of claim 68 which further comprises collecting monoclonal antibodies which specifically recognize GPVI from the monoclonal antibody-producing cell.

70. The method of claim 65 wherein the antibody specifically binds to an extracellular domain of the amino acid sequence of SEQ ID NO:3.

71. A monoclonal antibody or fragment thereof which specifically binds to a polypeptide of the amino acid sequence of SEQ ID NO:3, or the amino acid sequence encoded by the cDNA insert of the plasmid deposited with the ATCC as Accession Number 207180, wherein the antibody is a human, humanized or chimeric antibody.

72. The antibody of claim 71 which is conjugated to a therapeutic moiety.

73. The antibody of claim 71 which is linked to a detectable substance.

74. The antibody of claim 73, wherein the detectable substance is selected from the group consisting of an enzyme, a prosthetic group, a fluorescent material, a luminescent material, a bioluminescent material, and a radioactive material.

75. A kit comprising an antibody or fragment thereof as in claim 26, 87, 88, 89 or 90, and instructions for use.

76. A kit comprising an antibody or fragment thereof as in claim 27, and instructions for use.

77. A kit comprising an antibody or fragment thereof as in claim 29, and instructions for use.

78. A kit comprising an antibody or fragment thereof as in claim 71, and instructions for use.

79. A kit comprising an antibody or fragment thereof as in claim 73, and instructions for use.

87. The substantially purified non-human antibody of claim 26, wherein said antibody is at least 80% pure.

88. The substantially purified non-human antibody of claim 87, wherein said antibody is at least 90% pure.

89. The substantially purified non-human antibody of claim 88, wherein said antibody is at least 95% pure.

90. The substantially purified non-human antibody of claim 89, wherein said antibody is at least 99% pure.